# BRCA1/2 Testing in Hereditary Breast and Ovarian Cancer Families: Effectiveness of Problem-Solving Training as a Counseling Intervention

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It remains uncertain whether members of hereditary breast and ovarian cancer (HBOC) families experience psychological distress with genetic testing and whether pre-test counseling can have a moderating effect on client well-being. One purpose of this study was to assess change in psychological well-being from baseline to 6-9 months follow-up and the effect of a problem-solving training (PST) intervention on psychological well-being. Two hundred and twelve members of 13 HBOC families were offered BRCA1/2 testing for a previously identified family mutation. Participants received education and were randomized to one of two counseling interventions; PST or client-centered counseling. Psychological wellbeing was assessed at baseline and again at 6-9 months following the receipt of test results, or at the equivalent time for those participants who chose not to undergo testing. Well-being was assessed using measures of depressive symptoms (CESD), intrusive thoughts (IES), cancer worries, and self-esteem. Comparisons were made between those who chose testing and those who did not as well as between those who received positive and negative test results. One hundred eighty one participants elected to undergo genetic testing (85%) and 47 of these (26%) were identified as BRCA1/2 mutation carriers. Breast and ovarian cancer worries decreased significantly (p = 0.007and 0.008, respectively) in those who tested negative while there was no appreciable change in psychological well-being from baseline to follow-up in either those who tested positive or in non-testers. Among all participants, particularly testers, those randomized to PST had a greater reduction in depressive symptoms than

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those randomized to client-centered counseling (p < 0.05 and p = 0.02, respectively). Regardless of the decision to test, individuals with a personal history of cancer (n = 22) were more likely to have an increase in breast cancer worries compared to those who had never been diagnosed with cancer (p < 0.001). Results suggest that a problem-solving counseling intervention may help to enhance psychological well-being following testing and that a personal history of cancer may increase psychological distress associated with genetic testing. Published 2004 Wiley-Liss, Inc.

KEY WORDS: genetic counseling; hereditary breast and ovarian cancer; predictive genetic testing; counseling interventions; psychological well-being

## INTRODUCTION

Approximately, 1 in 20 women who develop breast cancer inherit a genetic predisposition in a breast cancer gene [Antoniou et al., 2001]. The two genes most commonly associated with hereditary breast and ovarian cancer (HBOC), BRCA1 and BRCA2 confer a 40-85% lifetime risk for developing breast cancer [Easton et al., 1995; Struewing et al., 1997; Ford et al., 1998; Hopper et al., 1999], and a 10-40% lifetime risk for developing ovarian cancer [Easton et al., 1997]. This study aimed to ascertain whether there were any changes in distress in members of HBOC families as a result of the decision to test, or test results and whether the type of counseling intervention had an effect on psychological well-being. Pre-test genetics education and counseling aim to promote informed choices and to minimize adverse consequences of testing. Assessing psychological distress in this population is important in anticipating who may most benefit from follow up counseling and because research suggests that psychological distress affects the degree to which individuals adhere to screening recommendations. A moderate degree of distress increases adherence while higher levels of anxiety appear to have an inhibiting effect [Lerman et al., 1991; Lerman and Rimer, 1993].

The discovery of BRCA1 led clinicians to contemplate the possible impact of genetic testing [Lerman et al., 1994a; Botkin et al., 1996]. When members of HBOC families were surveyed, expressed interest in testing was high and was found to be more strongly associated with heightened perceived vulnerability and cancer worries than actual degree of risk [Croyle and Lerman, 1993; Lerman et al., 1994b]. As testing became

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increasingly available studies were designed to ascertain whether the process itself and receipt of results were distressing for individuals from HBOC families [Lerman et al., 1994a; Botkin et al., 1996].

Studies compared level of distress prior to testing and shortly following receipt of results in HBOC families [Lerman et al., 1996; Croyle et al., 1997; Meiser et al., 2002]. When baseline distress was compared with that reported 1 week after receipt of test results, distress generally decreased although it was still high in carriers and particularly those carriers without a personal history of cancer [Croyle et al., 1997]. Lerman et al. [1996] compared depressive symptoms at baseline and at 1 month following receipt of results and found that non-carriers showed improvement in symptoms but carriers showed no change. In a separate study anxiety was measured at baseline, 1 and 6 months post-testing in an effort to identify individuals at increased risk for depression as a result of undergoing testing. Those with high anxiety levels at baseline were likely to have an increase in depressive symptoms if they declined testing, a decrease if they were tested and received a negative result or to have no change following a positive result [Lerman et al., 1998]. Lodder et al. [2001] measured anxiety and distress at pre-test and 1-3 weeks post receipt of test results in 78 healthy women from HBOC families. Non-carriers became less anxious and distressed from pre- to post-test and carriers showed a slight increase in psychological distress [Lodder et al., 2001].

Psychological well-being has also been studied in general breast cancer clinic patients who were offered BRCA1/2 testing. Findings from one study demonstrate that clinic patients who previously had cancer showed no change in psychological distress while their unaffected at-risk relatives had decreases following receipt of a negative result or no change after receiving a positive result [Schwartz et al., 2002]. In another study twenty-seven women were asked to anticipate their reactions to test results at baseline and their predictions were compared to their actual responses 6 months post results. They found that BRCA1 carriers with a personal history of cancer felt more anger at follow up than they had anticipated [Dorval et al., 2000]. Meiser et al. [2002] measured psychological wellbeing in 30 carriers and 60 non-carriers prior to testing and 1 week, 4 and 12 months after receipt of results. Similar to other studies they found that non-carriers showed a statistically significant decrease in depression scores from baseline to 12 months post results. However, contrary to previous studies, carriers appeared to have an increase in breast cancer distress which peaked at 1 week after receipt of results but remained increased over time [Meiser et al., 2002].

While studies to date suggest that distress seems not to increase around genetic testing, genetics education and counseling has not yet been evaluated for its role in maintaining psychological well-being. Problem-solving training (PST) has been shown to reduce stress in relatives of patients recently diagnosed with breast cancer [Schwartz et al., 1998]. This cognitive-behavioral intervention teaches people to select and implement the most effective coping strategies for a given stressor [D'Zurilla, 1988]. Schwartz et al. [1998] randomized first-degree relatives of breast cancer patients to one of two modes of counseling, including PST. Those participants who regularly practiced PST had greater reductions in cancerspecific distress than those who infrequently practiced it or those who were randomized to general health counseling. Further study of the same population revealed that for individuals with high levels of cancer-specific distress randomization to PST correlated with an increase in adherence to breast self-exam practices [Audrain et al., 1999]. This is a particularly important finding as studies to date suggest that increased distress can interfere with screening adherence [Lerman et al., 1991; Lerman and Rimer, 1993].

PST has been used in a number of different studies demonstrating its usefulness in constructive problem-solving, decreasing dysfunctional problem-solving and consequently positively affecting mood in the mothers of children recently diagnosed with cancer [Nezu et al., 1989; Wilson et al., 1995; Herrick and Elliott, 2001; Sahler et al., 2002]. This is the first known study to assess PST as an effective intervention for *BRCA1/2* genetics education and counseling.

#### Hypotheses

Based on previous studies, we hypothesized that,

- decision-making about BRCA1/2 testing would increase psychological distress among members of HBOC families
- declining testing would have more adverse effects on psychological well-being than choosing testing, because of the distress associated with decision-making itself
- a positive test result would be more likely to lead to increases in psychological distress
- individuals with a personal history of cancer would have less psychological distress as a result of testing
- the PST intervention would enhance coping with the stress of genetic testing.

## **METHODS**

## **Study Population**

Five hundred fifty nine letters of invitation were sent to all eligible adult (>18-years-old) men and women from 13 extended HBOC families in which BRCA1/2 mutations had been identified. There were 262 individuals who agreed to participate and completed the baseline questionnaire. Data from the 212 (81%) individuals who completed both the baseline and follow up questionnaires were analyzed for this study.

## Study Protocol

Family members who agreed to participate completed a baseline questionnaire prior to education and counseling that included measures of sociodemographics and psychological distress. A standardized (family) group education session was provided followed by an hour-long individual counseling session. Participants were randomized to receive an hour-long individual (or with a partner) counseling session, either a client-centered intervention or a problem-solving intervention as described below. Both those who opted for testing and those who declined testing were contacted for a telephone interview 6–9 months after results were received (or would have been given).

# **Description of the Intervention**

The client-centered intervention was modeled after common practices in genetic counseling that surround decision making for genetic testing, excluding genetics information and family history-taking [Kessler, 1979]. The intervention involved several open-ended questions and hypothetical inquiry into the possible outcomes of choosing or not choosing testing and the implications of receiving either test result. These sessions followed the expressed needs of the client but were guided by an outline for consistency. The outline included probes for expectations, concerns, and feelings associated with the decision to undergo testing.

PST is a cognitive-behavioral intervention that teaches people to select and implement the most effective coping strategies for a given stressor [D'Zurilla, 1988]. This method was applied with the assumption that the decision whether to

undergo testing was a stressor. If clients felt they already had made a decision, then they were encouraged to choose a challenge that they were concerned about related to their decision. The protocol included description of task-focused and emotion-focused coping and problem-solving, followed by a use of a checklist to identify the problem or challenge faced by the client, generation of solutions, solution evaluation, identification of barriers, decision-making, and plans for solution implementation [Schwartz et al., 1998]. The goals of this intervention were not only to facilitate test decision-making but also to teach clients effective strategies for coping with stress in the future. Providers involved in the study underwent training in administering the intervention in order to standardize delivery.

All education, counseling and testing were provided under an intramural National Institutes of Health research protocol (95-HG-0085) at no financial cost to participants. The National Cancer Institute Review Board approved the study protocol.

#### Measures

**Sociodemographics.** Participant data on gender, age, family membership, cancer history, education, employment status, income category, religious affiliation, and marital status were gathered.

## **Psychosocial Variables**

**Depression.** Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CESD). The CESD has adequate test-retest reliability (r=0.57 for 2-8 weeks) and was shown to relate to clinical ratings of the severity of depression [Radloff, 1977]. Possible scores on this measure range from 0 to 60, where higher scores reflect more depressive symptoms with 16 being the cutoff for clinical significance.

Self-esteem. Global self-esteem was assessed using the Rosenberg Self-Esteem Scale. It is a 10-item scale and scores were originally collapsed into a six point Guttman scale [Rosenberg, 1965]. It has most often been used in research as a simple summated scale, with 4- to 5-point Likert-type ratings [Tafarodi and Milne, 2002]. Therefore, a 5-point scale was used with responses ranging from strongly disagree to strongly agree. Scores range from 0 to 40 with higher scores reflecting higher levels of self-esteem. Cronbach's alpha coefficient has been reported as ranging from 0.76 to 0.87 with a test-retest reliability of 0.74 [Somerfield and Curbow, 1992].

Cancer-related distress. Cancer related symptoms were measured using the Impact of Events Scale (IES), the Breast Cancer Worries (BCW), and Ovarian Cancer Worries (OCW) Scales. The IES is a 15-item questionnaire designed to measure intrusive thinking and periods of avoidance as a result of a particular stressful life event [Horowitz et al., 1979]. The IES was used prior to the decision whether or not to undergo testing and again at follow-up to assess change in distress resulting from the decision to undergo testing and/or the test results. Each item is scored 0, 1, 3, or 5 with the higher scores reflecting more stressful impact. Scores below 25 are considered subclinical or mild while scores above 25 are considered moderate to severe. A number of separate sample studies have shown good internal consistency [Horowitz et al., 1979; Corcoran and Fischer, 1994] with a Cronbach's alpha of 0.78 to 0.82, and good test-retest reliability of 0.87 [Horowitz et al., 1979].

Lerman et al. [1994b] developed four Likert-style items to assess breast cancer worries. These include the frequency of breast cancer worries, the impact of worries on mood, and the impact on daily functioning (1, rarely or never; 2, sometimes; 3, often; 4, all the time). The level of breast cancer worry was similarly assessed. These four items were summed to create a

breast cancer worries scale. The ovarian cancer worries scale included the same questions modified to refer to ovarian cancer.

# **Statistical Analysis**

Paired t-tests and ANOVAs were used to assess associations between the socio-demographic variables and change in psychosocial variables. Linear regression was used to model the 6–9 month follow-up scores as a function of the baseline scores, test results (or testing status), gender, marital status, cancer-history and intervention group. One model examined differences between testers versus non-testers and the other examined differences between those who tested positive versus those who tested negative.

In addition, to ascertain whether baseline distress levels were associated with depression at follow up, the Intrusion subscale was categorized into two levels: low-stress (scores ranging from 1 to 7—lowest two tertiles) and high-stress (scores ranging from 8 to 41—highest tertile). Clinically significant levels of depressive symptoms are defined as having a CESD score of at least 16. Fishers' Exact tests were used to assess the association between baseline and follow-up depression and study groups stratified by stress level. Logistic regression models were used to associate follow-up depression and study groups after adjusting for baseline depression and possible confounding variables (sex, marital status, intervention, and previous cancer diagnosis). The models were stratified by stress level and robust standard errors were calculated which allow for possible correlation among persons from the same family. Interpretation of statistical significance was based on a  $p \le 0.05$ . Analyses were performed using STATA (version 7).

#### RESULTS

Two hundred twelve participants were assessed at both baseline and 6–9 month follow-up. There were no statistical differences in sociodemographics, testing decision or test results between those who completed only the baseline questionnaire and those who completed both baseline and follow up questionnaires in terms of the decision to be tested and test results. A description of the sociodemographics and genetic testing status of the 212 individuals who completed both questionnaires is presented in Table I. Participants were primarily Caucasian and well-educated.

# **Univariate Analysis**

Table II summarizes the data on psychological scores at baseline and at 6–9 months follow-up for those participants with a positive test result, a negative test result and for those participants who did not elect to undergo the genetic testing. Psychological well-being improved significantly for those who received a negative result as demonstrated by a reduction in intrusive thoughts ( $p\!=\!0.005$ ), depressive symptoms ( $p\!=\!0.04$ ), and breast and ovarian cancer worries ( $p\!<\!0.001$ ) from baseline to follow up. In those who tested positive and those who declined testing, there were no significant changes in psychological well-being.

Prior to generating the regression models, we performed univariate analyses to identify covariates (variables associated with an outcome at p < 0.10). This suggested that marital status was statistically significantly related to baseline and follow-up CESD (p = 0.002 and 0.064, respectively). Religion was associated with baseline CESD (p = 0.083) and breast cancer worries (p = 0.089) and follow-up IES (p = 0.060) and self-esteem (p = 0.001). Employment status was associated with baseline IES (p = 0.057), breast cancer worries

TABLE I. Summary Statistics

Variable	Level	Count (%) 95 (45)	
Age	Under 40		
	40 and above	117 (55)	
Gender	Female	138 (65)	
	Male	74 (35)	
Marital status	Married	129 (61)	
	Single, widowed, separated, divorced	56 (26)	
	Missing	27(13)	
Employment status	Employed	124 (58)	
• •	Unemployed, retired, employed part time	88 (42)	
Income category	Less than \$35,000	57 (27)	
<b>.</b>	\$35,000 or above	153 (72)	
	Missing	2(1)	
Religious affiliation	Protestant	99 (47)	
C	Catholic	40 (19)	
	Jewish	54 (25)	
	Other	8 (4)	
	None	8 (4)	
Intervention	Client-centered	109 (51)	
	Problem-solving	103 (49)	
Genetic testing	Yes	181 (85)	
S	No	31 (15)	
Result given genetic testing	Positive	47 (26)	
5 5 8	Negative	134 (74)	

(p=0.100) and ovarian cancer worries (p=0.090) and follow-up self-esteem (p=0.003). Income level was associated with baseline CESD (p=0.015), self-esteem (p=0.057), and breast cancer worries (p=0.034).

Multiple linear regression models suggested that the differences between testers and non-testers were not sensitive to adjustment for the confounding variables: gender, marital status, employment status, religious affiliation, and income level. The same was true when analysis was performed comparing those who tested positive with those who tested negative.

#### **Multivariate Analysis**

Tables III and IV include change in psychological well-being between testers to non-testers, and those who tested positive and those who tested negative, adjusting for baseline scores, intervention, gender and marital status. Table III demonstrates that testers had greater improvements than nontesters in breast cancer worries (p=0.015). Regardless of the decision to test, individuals with a personal history of cancer

had a significantly greater increase in breast cancer worries (p < 0.001). Individuals who had received problem-solving counseling had greater reductions in their depressive symptoms at follow up than those who received client-centered counseling (p = 0.052) regardless of their testing decision.

Table IV includes only subjects who chose to be tested and demonstrates that individuals who received a negative result for BRCA1/2 had a significantly greater reduction in both breast and ovarian cancer worries (p=0.008 and 0.007, respectively) than those individuals who tested positive. Regardless of test results, individuals with a personal history of cancer had a significant increase in breast cancer worries compared to individuals who had never been diagnosed with cancer (p<0.001). Finally, in all individuals tested, those who received the PST had a significantly greater decrease in their CESD score than those who received client-centered counseling (p=0.021).

There was no significant association between those with lowlevel versus high-level intrusive thoughts at baseline and change in CESD score comparing those who tested positive, negative and those who declined testing.

TABLE II. Mean and Standard Deviation of Psychological Well-Being Comparing Baseline and 6-9 Months Follow-Up

Measure	Outcome	Baseline	6-9 months follow-up	<i>p</i> -value
Impact of events (intrusive thoughts)	Positive test	23.10 (1.29)	23.00 (1.42)	0.955
•	Negative test	24.79(0.77)	21.25(0.73)	< 0.001
	Non-tester	23.45 (1.59)	20.17 (1.77)	0.188
CESD	Positive test	8.11 (1.23)	8.11 (1.60)	1.000
	Negative test	7.36 (0.60)	5.97 (0.63)	0.037
	Non-tester	6.50(1.26)	7.39 (1.89)	0.592
Self-esteem	Positive test	35.29 (0.75)	35.48 (0.60)	0.797
	Negative test	34.41 (0.36)	34.69 (0.35)	0.055
	Non-tester	36.76 (0.76)	35.40 (0.76)	0.142
Breast cancer worries	Positive test	4.54 (0.17)	4.61 (0.25)	0.823
	Negative test	4.08 (0.12)	3.10 (0.09)	< 0.001
	Non-tester	4.06 (0.21)	4.00 (0.23)	0.804
Ovarian cancer worries	Positive test	3.79 (0.29)	3.86 (0.30)	0.870
	Negative test	3.63 (0.15)	2.72 (0.10)	< 0.001
	Non-tester	3.83 (0.25)	3.28 (0.25)	0.056

TABLE III. Regression Analysis Comparing Change in Psychological Measures for Testers Versus Non-Testers

Outcome	Variables	Levels	Beta	p	$\mathrm{Adj.}\ \mathrm{R}^2$
Impact of events	Baseline IOE		0.05 (0.07)	0.494	-0.008
At 6–9 months	Gender	Female	1.07 (1.73)	0.551	
	Marital status	Married	-2.10(1.26)	0.124	
	Cancer history	Yes	1.90 (2.22)	0.410	
	Intervention	Client-center	-0.40(1.32)	0.768	
	Testing	Yes	1.84 (1.55)	0.261	
CESD <sup>a</sup>	Baseline CESD		0.54(0.12)	< 0.001	0.211
At 6–9 months	Gender	Female	-0.84(1.26)	0.520	
	Marital status	Married	-0.78(1.58)	0.632	
	Cancer history	Yes	4.10 (2.20)	0.089	
	Intervention	Client-center	2.38 (1.09)	0.052	
	Testing	Yes	-1.94(2.63)	0.477	
Self-esteem	Baseline SE		0.37(0.05)	< 0.001	0.142
At 6–9 months	Gender	Female	-0.61(0.55)	0.293	
	Marital status	Married	0.10(0.71)	0.888	
	Cancer history	Yes	-0.0092 (0.60)	0.988	
	Intervention	Client-center	-0.23(0.48)	0.631	
	Testing	Yes	-0.06(0.80)	0.945	
BRCA worries	Baseline BRCA worries		0.23(0.09)	0.030	0.259
At 6–9 months	Marital status	Married	-0.15(0.23)	0.524	
	Cancer history	Yes	1.58(0.27)	< 0.001	
	Intervention	Client-center	0.16(0.19)	0.413	
	Testing	Yes	-0.58(0.28)	0.063	
OVCA <sup>a</sup> worries	Baseline OVCA worries		0.20(0.12)	0.120	0.060
At 6–9 months	Marital status	Married	-0.25(0.24)	0.312	
	Cancer history	Yes	0.63(0.39)	0.139	
	Intervention	Client-center	0.17(0.09)	0.119	
	Testing	Yes	$-0.14\ (0.34)$	0.696	

 $<sup>^{\</sup>rm a}{\rm Standard}$  errors are adjusted for within family correlations.

TABLE IV. Regression Analysis Comparing Change in Psychological Measures for Those Receiving Positive Versus Negative Results

Outcome	Variables	Levels	Beta	p	$\mathrm{Adj.}\ \mathrm{R}^2$
Impact of events	Baseline IOE		0.07 (0.09)	0.446	-0.008
At 6–9 months	Gender	Female	1.42 (1.90)	0.468	
	Marital status	Married	-2.22(1.26)	0.105	
	Cancer history	Yes	2.22(3.90)	0.581	
	Intervention	Client-center	0.60(1.78)	0.741	
	Test	Positive	0.35(2.76)	0.903	
$CESD^a$	Baseline CESD		0.48(0.10)	0.001	0.224
At 6–9 months	Gender	Female	-1.29(1.36)	0.362	
	Marital status	Married	-1.95(1.52)	0.225	
	Cancer history	Yes	2.86 (2.99)	0.359	
	Intervention	Client-center	3.25 (1.16)	0.017	
	Test	Positive	0.31(1.45)	0.832	
Self-esteem	Baseline SE		0.38(0.07)	< 0.001	0.167
At 6–9 months	Gender	Female	-0.03(0.53)	0.957	
	Marital status	Married	0.62(0.76)	0.433	
	Cancer history	Yes	-0.34(1.04)	0.751	
	Intervention	Client-center	-0.09(0.63)	0.887	
	Test	Positive	1.16(0.70)	0.124	
BRCA worries	Baseline BRCA worries		0.15(0.09)	0.118	0.370
At 6–9 months	Marital status	Married	-0.11(0.25)	0.677	
	Cancer history	Yes	1.04 (0.35)	0.012	
	Intervention	Client-center	0.21(0.12)	0.106	
	Test	Positive	1.03 (0.35)	0.013	
OVCA <sup>a</sup> worries	Baseline OVCA worries		0.18 (0.11)	0.149	0.194
At 6–9 months	Marital status	Married	-0.14(0.25)	0.586	
	Cancer history	Yes	0.22(0.48)	0.657	
	Intervention	Client-center	0.20(0.11)	0.099	
	Test	Positive	1.05 (0.42)	0.031	

 $<sup>^{\</sup>rm a} Standard \, {\rm errors}$  are adjusted for within family correlations.

#### DISCUSSION

We hypothesized that making a decision about *BRCA1/2* testing would increase psychological distress among members of HBOC families. This appeared to be true for individuals with a personal history of cancer who demonstrated an increase in breast cancer worries regardless of their decision to test. Consistent with results from other studies, this suggests there may be subgroups of cancer families who are particularly vulnerable to distress and worthy of targeted clinical intervention [Lerman et al., 2002]. Although, it is also worth noting that baseline levels of anxiety amongst participants were similar to those seen in women being treated for cancer, suggesting some anxiety associated with testing may have already been present at baseline [Manne et al., 2001].

In conjunction with our hypothesis that declining testing may have more adverse effects on psychological well-being, we looked to see whether there was a higher follow up depression level in decliners who had high intrusive thoughts. Unlike Lerman et al. [1998] and contrary to our prediction, we did not find that decliners with higher levels of intrusive thoughts at baseline were more likely to be depressed at follow up. This may be partly due to the fact that the previous study looked at depression levels 1 month following receipt of results whereas our study did not ascertain depressive symptoms again until 6–9 months after test results had been (or would have been) received. This explanation would be consistent with the study by Meiser et al. [2002] which showed that depression peaked 1 week post testing and gradually decreased thereafter.

A "true" negative test result was associated with a significant decrease in breast and ovarian cancer worries and these findings are consistent with previous research [Lerman et al., 1996; Lodder et al., 2001; Meiser et al., 2002] suggesting that non-carriers experience relief following receipt of a negative test result. Contrary to our hypothesis, a positive test result did not lead to an increase in distress. Data and opinions are less certain about distress in  $BRCA\ 1/2$  carriers as one study has shown a significant increase with time [Meiser et al., 2002] while others have shown no change in distress [Lerman et al., 1996; Lodder et al., 2001]. It seems that either genetic testing is no more stressful than living at increased cancer risk within HBOC families or that the measures that have been used to ascertain distress are not sufficiently sensitive to detect it.

# **Counseling Model**

PST did prove to be more effective in improving psychological well-being among HBOC family members in this study. Indeed, regardless of the testing decision or the result, the decrease in depressive symptoms was significantly greater in those who received PST than those who participated in clientcentered counseling. This finding is consistent with empirical evidence that the use of cognitive coping strategies mediates the effects of stressful life events, such as a health threat [Lazarus and Folkman, 1984]. PST offers HBOC family members a structured opportunity to consider the choices available to them and to anticipate the consequences of a variety of different outcomes. By enhancing the likelihood that these clients make a thorough decision, there is a chance that anticipating the consequences may allow some to avoid making decisions they may later regret. It also invests the client more concretely in the process of making a decision about genetic testing.

Our findings suggest that PST may successfully maintain psychological well-being in clients undergoing genetic testing. This has implications for genetic counseling practice as a means to enhance decision-making for genetic testing. Cognitive psychotherapy interventions may hold promise in genetic

counseling as a means to maximize psychological well-being among those faced with or living with genetic test results.

## **Cancer History**

A personal history of breast cancer was significantly associated with one's breast cancer worries regardless of the decision to undergo testing. Those participants who had previously been diagnosed with cancer and chose genetic testing, regardless of their result, had significant increases in their breast cancer worries compared to participants who had no personal history of cancer. Schwartz et al. [2002] found no change in distress levels among women with a personal history of cancer following BRCA1/2 testing. Their research participants differed from those in this study as the women were not members of HBOC families and the familial mutation had not been previously identified and it is possible that disease perception and the meaning of test results differed between these populations. A study of distress in women with a family history of breast/ovarian cancer who sought testing showed that women who previously had cancer had significantly higher levels of ovarian cancer worries 12 months after genetic counseling than other women at increased risk [Bish et al., 2002]. In a more similar population of sixty women who were members of a single HBOC family, distress was greatest 1-2 weeks after receiving test results in carriers who had never been diagnosed with cancer [Croyle et al., 1997]. Since distress was not measured at baseline in this study we do not know whether there were significant changes in distress. When forty-one members of HBOC families were tested in another study, it was found that of the seventeen identified carriers, the seven with a personal history of cancer experienced greater levels of anger and worry than they had anticipated prior to testing [Dorval et al., 2000]. Findings from these studies conflict and it remains unclear whether cancer history predicts greater psychological distress. Our results suggest that it does in members of HBOC families and particular attention ought to be given in genetic counseling to these clients and their potential need for follow-up counseling.

# **Study Limitations**

There were several limitations to our study. The findings are not generalizable to all HBOC families who have been offered *BRCA1/2* testing. This is a highly educated and predominately Caucasian population. Overall, participants demonstrated elevated levels of baseline anxiety. There were greater numbers of those who chose testing and those with negative results, resulting in comparisons among disproportionately sized groups. Those who agreed to participate in the study were part of a prior research population that had indicated significant prior interest in genetic testing.

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## REFERENCES

Antoniou AC, Pharoah PD, McMullan G, Day NE, Ponder BA, Easton D. 2001. Evidence for further breast cancer susceptibility genes in addition

- to BRCA1 and BRCA2 in a population-based study. Genet Epidemiol 21:1-18.
- Audrain J, Rimer B, Cella D, Stefanek M, Garber J, Pennanen M, Helzlsouer K, Vogel V, Lin TH, Lerman C. 1999. The impact of a brief coping skills intervention on adherence to breast self-examination among first-degree relatives of newly diagnosed breast cancer patients. Psychooncology 8: 220–229.
- Bish A, Sutton S, Jacobs C, Levene S, Ramirez A, Hodgson S. 2002. Changes in psychological distress after cancer genetic counselling: A comparison of affected and unaffected women. Br J Cancer 86:43–50.
- Botkin JR, Croyle RT, Smith KR, Baty BJ, Lerman C, Goldgar DE, Ward JM, Flick BJ, Nash JE. 1996. A model protocol for evaluating the behavioral and psychosocial effects of BRCA1 testing. J Natl Cancer Inst 88:872–882.
- Corcoran K, Fischer J. 1994. Measures for clinical practice: A sourcebook, Vol 2. New York: The Free Press.
- Croyle RT, Lerman C. 1993. Interest in genetic testing for colon cancer susceptibility: Cognitive and emotional correlates. Prev Med 22:284– 292.
- Croyle RT, Smith KR, Botkin JR, Baty B, Nash J. 1997. Psychological responses to BRCA1 mutation testing: Preliminary findings. Health Psychol 16:63–72.
- D'Zurilla TJ. 1988. Problem-solving therapy: A social competence approach to clinical intervention. New York: Springer.
- Dorval M, Patenaude AF, Schneider KA, Kieffer SA, DiGianni L, Kalkbrenner KJ, Bromberg JI, Basili LA, Calzone K, Stopfer J, Weber BL, Garber JE. 2000. Anticipated versus actual emotional reactions to disclosure of results of genetic tests for cancer susceptibility: Findings from p53 and BRCA1 testing programs. J Clin Oncol 18:2135-2142.
- Easton DF, Ford D, Bishop DT. 1995. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Am J Hum Genet 56:265–271.
- Easton DF, Steele L, Fields P, Ormiston W, Averill D, Daly PA, McManus R, Neuhausen SL, Ford D, Wooster R, Cannon-Albright LA, Stratton MR, Goldgar DE. 1997. Cancer risks in two large breast cancer families linked to BRCA2 on chromosome 13q12-13. Am J Hum Genet 61:120–128
- Ford D, Easton DF, Stratton M, Narod S, Goldgar D, Devilee P, Bishop DT, et al. 1998. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. Am J Hum Genet 62:676–689.
- Herrick SM, Elliott TR. 2001. Social problem-solving abilities and personality disorder characteristics among dual-diagnosed persons in substance abuse treatment. J Clin Psychol 57:75–92.
- Hopper J, Southey M, Dite G, Jolley D, Giles G, McCredie M, Easton D, Venter D. 1999. Population-based estimate of the average age-specific cumulative risk of breast cancer for a defined set of protein-truncating muations in BRCA1 and BRCA2. Australian Breast Cancer Family Study. Cancer Epidemiol Biomarkers Prev 8:741–747.
- Horowitz M, Wilner N, Alvarez W. 1979. Impact of event scale: A measure of subjective stress. Psychosom Med 41:209–218.
- Kessler S. 1979. Genetic counseling: Psychological dimensions. London: Academic Press, Inc.
- Lazarus RS, Folkman S. 1984. Stress, appraisal, and coping. New York: Springer.
- Lerman CE, Rimer BK. 1993. Psychosocial impact of cancer screening. Oncology (Huntingt) 7:67–72; discussion 72, 75, 79.
- Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. 1991.
  Psychological side effects of breast cancer screening. Health Psychol 10:259-267.

- Lerman C, Audrain J, Croyle RT. 1994a. DNA-testing for heritable breast cancer risks: Lessons from traditional genetic counseling. Ann Behav Med 16:327–333.
- Lerman C, Daly M, Masny A, Balshem A. 1994b. Attitudes about genetic testing for breast-ovarian cancer susceptibility. J Clin Oncol 12:843–850.
- Lerman C, Narod S, Schulman K, Hughes C, Gomez-Caminero A, Bonney G, Gold K, Trock B, Main D, Lynch J, Fulmore C, Snyder C, Lemon SJ, Conway T, Tonin P, Lenoir G, Lynch H. 1996. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. JAMA 275:1885–1892.
- Lerman C, Hughes C, Lemon SJ, Main D, Snyder C, Durham C, Narod S, Lynch HT. 1998. What you don't know can hurt you: Adverse psychologic effects in members of BRCA1-linked and BRCA2-linked families who decline genetic testing. J Clin Oncol 16:1650–1654.
- Lerman C, Croyle RT, Tercyak KP, Hamann H. 2002. Genetic testing: Psychological aspects and implications. J Consult Clin Psychol 70:784–797.
- Lodder L, Frets PG, Trijsburg RW, Meijers-Heijboer EJ, Klijn JG, Duivenvoorden HJ, Tibben A, Wagner A, van der Meer CA, van den Ouweland AM, Niermeijer MF. 2001. Psychological impact of receiving a BRCA1/BRCA2 test result. Am J Med Genet 98:15–24.
- Manne S, Glassman M, Du Hamel K. 2001. Intrusion, avoidance, and psychological distress among individuals with cancer. Psychosom Med 63:658–667.
- Meiser B, Butow P, Friedlander M, Barratt A, Schnieden V, Watson M, Brown J, Tucker K. 2002. Psychological impact of genetic testing in women from high-risk breast cancer families. Eur J Cancer 38:2025– 2031.
- Nezu AM, Nezu CM, Perri MG. 1989. Problem-solving therapy for depression: Theory, research, and clinical guidelines. New York: Wilay
- Radloff L. 1977. The CES-D Scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1:385–401.
- Rosenberg M. 1965. Society and the adolescent self-image. Princeton, New Jersey: Princeton University Press.
- Sahler OJ, Varni JW, Fairclough DL, Butler RW, Noll RB, Dolgin MJ, Phipps S, Copeland DR, Katz ER, Mulhern RK. 2002. Problem-solving skills training for mothers of children with newly diagnosed cancer: A randomized trial. J Dev Behav Pediatr 23:77–86.
- Schwartz MD, Lerman C, Audrain J, Cella D, Rimer B, Stefanek M, Garber J, Lin TH, Vogel V. 1998. The impact of a brief problem-solving training intervention for relatives of recently diagnosed breast cancer patients. Ann Behav Med 20:7–12.
- Schwartz MD, Peshkin BN, Hughes C, Main D, Isaacs C, Lerman C. 2002. Impact of BRCA1/BRCA2 mutation testing on psychologic distress in a clinic-based sample. J Clin Oncol 20:514–520.
- Somerfield M, Curbow B. 1992. Methodological issues and research strategies in the study of coping with cancer. Soc Sci Med 34:1203– 1216.
- Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams M, Timmerman MM, Brody LC, Tucker MA. 1997. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. N Engl J Med 336:1401–1408.
- Tafarodi RW, Milne AB. 2002. Decomposing global self-esteem. J Pers 70:443-483.
- Wilson KG, Stelzer J, Bergman JN, Kral MJ, Inayatullah M, Elliott CA. 1995. Problem solving, stress, and coping in adolescent suicide attempts. Suicide Life Threat Behav 25:241–252.